REMARKS/ARGUMENTS

Claims 1, 2, 7, 9-12, 23-25 and 31 were pending in this application.

Claims 1, 2, 7, 9 and 25 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lawless et al. US 5,586,868 in view of Epstein et al. US 5,464,392 and Jeon et al. US 20020168278. This rejection is respectfully traversed for the reasons that follow.

Claim 7 has been cancelled without prejudice. Claims 1 and 25 have been amended to include the limitations of claim 7 and to provide greater clarity about the closed loop feedback aspect of the present invention. Claims 1 and 25 have been amended to clarify that the stroke frequency of the pump is modified or adjusted for a future or subsequent stroke based on the calculated actual stroke volume of at least one past stroke that actually attempted fluid delivery. Fluid delivery cannot be attempted without actually attempting to open the outlet valve as described in the last few lines of claims 1 and 25. Claim 25 has also been amended to recite that the ~~pumping element~~plunger is operatively associated with a shaft and the pressure sensor is directly connected to the plunger and positioned in-line with the plunger between the pumping chamber and the shaft. The amendments to claim 1 are supported by the original specification at pages 12 and 13. The last mentioned amendments to claim 25 are supported on page 8, lines 5-19 of the original specification. Thus, no new matter has been added.

Even in the wake of the *KSR* decision, under the USPTO guidelines the Examiner must at least provide a logical rationale for combining the references and an explanation of how the claimed invention results from the combination. Here, the Examiner has failed to meet that burden and establish a prima facie case of obviousness. Instead, the Examiner seems to have resorted to the impermissible use of hindsight in view of the instant application to reconstruct the claimed invention. Since the rejections of all of the claims are based on the foundational combination of Lawless et al. '868, Epstein et al. '392, and Jeon et al. US 20020168278, it is appropriate to begin by looking closely at those three references for any teaching they might reasonably provide about amended claim 1.

Lawless et al. '868 discloses a medical pump for use with a cassette having a pumping chamber 22. The pump cassette has a passive inlet valve 49a and a passive outlet valve 49b, but item 30b is a part of a flow stop/pressure monitoring member 24 located on the cassette downstream of the outlet valve 49b and pumping chamber 22. Item 30b is not "a plunger adapted to intermittently pressurize the pumping chamber during the pumping cycle," as

required by claim 1. Instead, the plunger in Lawless et al. '868 is discussed in column 6, lines 47-49 and is designated with reference numeral 73 in FIGS. 7 and 8. Lawless also discloses proximal and distal pressure sensors 74, 75 in FIGS. 7 and 8 that are remote from the plunger or pumping element. Armed with a correct understanding of the components of Lawless et al., it is clear that Lawless et al. fail to disclose "a pressure sensor directly connected to the plunger and adapted to detect the pressure exerted by the plunger on the pumping chamber" as required by claim 1. Consequently and most importantly, Lawless lacks a memory containing "programming code executed by the processing unit to establish an expected nominal stroke volume associated with the attempted fluid delivery stroke of the pump, set a first stroke frequency based upon a desired dosage rate and the expected nominal stroke volume, thence, during pressurization of the pumping chamber for at least one attempted fluid delivery stroke, process pressure data from the pressure sensor and position data from the position sensor to determine a calculated actual stroke volume of the pump for the pumping cycle, and, if the calculated actual stroke volume is greater than a given threshold value, to modify the first stroke frequency to a second stroke frequency different than the first stroke frequency in order to compensate for variation between the calculated actual stroke volume and the expected nominal stroke volume so as to more closely approach the desired dosage rate during a subsequent pumping cycle." The present invention uses the pressure and position data to calculate the actual stroke volume for each pumping cycle, compares it to the expected nominal stroke volume, and in response adjusts the stroke frequency in a closed loop manner so that the actual dosage rate (stroke volume times stroke frequency) might more closely approach the desired dosage rate for a subsequent pumping cycle and over time.

Epstein et al. '392 discloses an infusion system that utilizes a unitary disposable cassette and multiple active valves to deliver multiple infusates at individually programmable rates, volumes and sequences from plural fluid ports. The system is supposedly operative to adapt actual to desired flow rates in normal operation. Air bubbles are automatically detected and disposed of. Fluid pressures are monitored and system operation adjusted (before each stroke) as a function of such pressures. (Abstract) However, a closer examination reveals some key differences between the system and method of Epstein et al. and the presently claimed invention.

First, Epstein et al. disclose a pump chamber 20/208 intermittently stroked by first plunger or pumping actuator 46/272 in FIGS. 1, 4 and 5 and a separate pressure chamber

22/212 located downstream of the pump chamber 20 and outlet valve via a passageway. A pressure head 306 fastened to a pressure transducer 40 on linkage 310 monitors pressure at the pressure chamber 22/212 (C19, L30-39), <u>not directly at the pumping plunger</u> or pump chamber 20. The pressure reading is subject to variations due to cassette installation and manufacturing tolerances, the geometry of the intervening passageway, and may not accurately reflect the true pressure in the pump chamber 20 or its fluctuation over time. Furthermore, the pressure head 306 is only monitoring the pressure at the pressure chamber 22/212 and is not motorized to act as a plunger on the chamber 22/212

Second, Epstein et al. disclose a system that relies on actively controlled valves. In particular, active inlet and outlet valves 18, 28 are required. These valves require actuator mechanisms 34 to operate them. (C5, L55-67) In fact, as best seen in FIGS. 5 and 6, a second motor and cam system is required to operate the valves. The active valves, valve operating mechanisms, and separate pressure chamber/sensor mechanism increase the size and complexity of both the cassette and the pump.

Finally, Epstein et al. disclose a method of processing data from the pressure sensor and position sensor that is different from the present invention. Epstein et al. require pre-pumping steps to determine the amount of air in the cassette and reach a certain pressure threshold before an actual attempted fluid delivery cycle will occur. This method of front end plunger extension and retraction in a trial manner with the inlet and outlet valves closed, then calculation of estimated stroke volume and the setting of stroke frequency prior to actual delivery is an open loop, forward looking approach that involves many delays that cannot be afforded, particularly in low flow situations. Furthermore, there is no looking back or closed loop feedback to see what the actual stroke volume was during the actual delivery cycle when the outlet valve is open. Such information is not collected or taken into account for the next pumping cycle or stroke. Instead, the pre-pumping steps and calculations are repeated anew before the next pumping cycle. The present invention identifies when the outlet valve opens and calculates the actual volume delivered per stroke. This calculated actual volume is compared to a target or expected nominal stroke volume and is used to adjust the stroke frequency in a closed loop manner.

One skilled in the art would be disinclined to combine the teaching of Epstein et al. and Lawless et al. because Lawless et al. already has a downstream pressure sensing mechanism (30, 30b and distal pressure sensor 75), so there is no compelling reason to supplement or replace it with a similar but bulkier and costlier downstream pressure sensing

mechanism. Furthermore, without destroying the cost and simplicity advantages of the passive inlet and outlet valves of Lawless et al. and using the more expensive, bulky and complex active valves of Epstein et al., the Applicants have discovered that it is extremely difficult to know precisely when in the pumping cycle the passive outlet valve has actually opened and the actual pressure conditions and stroke volume in the pumping chamber itself during pressurization. A downstream pressure sensor like taught by Epstein et al. and Lawless et al. necessarily introduces a time lag and opportunities for inaccuracies, especially at low flow rates.

The Examiner seems to recognize that Epstein et al. require knowledge of the state of the valves in the pump to apply their control algorithm and that such knowledge is missing in the pump of Lawless et al. The Examiner cites paragraph 128 of Jeon et al. as teaching a method for determining the state of a passive valve 30 including processing pressure data to indicate when a valve has opened. However, the paragraph cited merely discusses an example of experiments run on one-use passive microfluidic valves to determine the effect of applied voltage on the valve opening size and minimum pulse lengths of the voltages. The photographs of FIGS. 30-33 show the fluid flowing through the valves when various voltages are applied in the manner described. Jeon et al. does not teach a mechanical plunger adapted pressurize a pumping chamber and a pressure sensor directly connected to the plunger to monitor pressure in a closed pumping chamber to indicate when a passive outlet valve opens. Jeon et al. disclose a valve that is passive only in the sense that it is not mechanically operated. It appears from the cited paragraph that a voltage must be applied to electrodes on either side of the valve to cause the valve to open. And even if Jeon et al. does teach pressure sensing in a pumping chamber with a passive outlet valve, the combination still does not teach the plunger and pressure sensor arrangement, the particular use of that pressure information, or the closed loop feedback aspects of the present invention that are missing in Lawless et al. and Epstein et al. Thus, amended claim 1 is believed to be patentable. Claims 2, 9-12, and 31 depend from claim 1 and at least derive their patentability therefrom.

Amended claim 25 has many of the same limitations discussed above with respect to claim 1 and thus is believed to be patentably distinct from Lawless et al. in view of Epstein et al and Jeon et al. for at least the reasons discussed above.

Claims 10-11, 23 and 24 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lawless et al. '868 in view of Epstein et al. '392 and in view of Jeon et al. as applied to claim 9 above, and further in view of Madsen et al. US 4,850,805. This rejection is

respectfully traversed at least for the same reasons stated above relative to claim 1. Claim 23 has been amended in many of the same ways as claim 1, such that claims 23 and 24 are believed to be patentable. Madsen et al. US 4,850,805 has a pair of capacitor plates 64, 66 and force sensing circuitry 100 that is indirectly connected to the plunger 74 by virtue of an intervening pivot connection 62, sensing beam 70 and flexible beam 68. Madsen et al. does not cure all of the shortcomings of the primary, secondary and tertiary references.

Claims 12 and 31 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lawless et al. '868 in view of Epstein et al. '392, Jeon et al. '278, and Madsen et al. '805 as applied to claim 10 above, and further in view of Holst et al. US 20030055375. This rejection is respectfully traversed at least for the reasons stated above relative to claim 1. Holst et al. US 20030055375 discloses reliance on proximal and distal pressure sensors 24, 34 that are remote from the plunger 42 and fails to cure all of the shortcomings of the other references.

A Petition for Extension of Time by three (3) months from July 30, 2008 to October 30, 2008 is submitted herewith along with the authorization for payment of the appropriate fees. No further extensions or fees are believed to be due in connection with this paper. However, the Commissioner is authorized to consider this a request for any necessary extension and charge our Deposit Account, 50-3118 for any additional fees (or credit any over payments) in association with this communication.

This amendment is being submitted with a Request for Continued Examination. A timely and favorable response on the merits of the claims as amended is respectfully requested.

Respectfully submitted,
M. W. Lawless, et al.

41155 Customer No.

Hospira, Inc
Telephone: (224) 212-2889
Facsimile: (224) 938-2088

/MRC/
Michael R. Crabb
Registration No. 37,298
Attorney for Applicants